

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application.

1. (currently amended) ~~A composition~~ An antigenic composition comprising a heterologous antigen linked to the amino acid sequence set forth in SEQ ID NO:38, ~~said amino acid sequence comprising a loop region~~ wherein said heterologous antigen and said amino acid sequence assemble as a hybrid particle.

2. (currently amended) The composition of Claim 1, wherein said heterologous antigen is inserted at a position ~~within said~~ within a loop region comprising residues 76 to 82 of SEQ ID NO:38.

3. (currently amended) The composition of Claim 2, wherein said position within said loop region is chosen from amino acid residues 77, 78, 81, ~~and 82~~ or 82.

4. (original) The composition of Claim 2, wherein said position within said loop region is at amino acid residue 76.

5. (canceled)

6. (currently amended) The composition of Claim 5, ~~wherein said position outside said loop region is 1,~~ wherein said heterologous antigen is inserted at a position chosen from amino acid residues ~~71, 72, 73, 74, 75, 83, 84, 85, 92, 73, 75, N-terminal and C-terminal~~ or C-terminal.

7. (currently amended) The composition of Claim 5, ~~wherein said position outside said loop region is at amino acid residue 44~~ 1, wherein said heterologous antigen is inserted at a position chosen from amino acid residues 44, 71, 72, 74, 83, 84, 85, or 92.

8. (currently amended) The composition of Claim 1, wherein said heterologous antigen is inserted at a position ~~within said~~ within a loop region comprising residues 76 to 82 of SEQ ID NO:38, and in a position outside said loop region.

9. (original) The composition of Claim 1, wherein said heterologous antigen is conjugated to said amino acid sequence.

10. (original) The composition of Claim 1, wherein said heterologous antigen comprises at least one B cell epitope.

11. (original) The composition of Claim 1, wherein said heterologous antigen comprises at least one T helper cell epitope.

12. (currently amended) The composition of Claim 1, wherein said amino acid sequence further comprises an artificial C-terminus of from 1 to 100 amino acids at the carboxy end of residue I¹⁴⁹.

13. (currently amended) The composition of Claim 12, wherein said 1 to 100 amino acids is chosen from R^{150} , E^{150} , K^{150} , A^{150} , $R^{150}R^{151}C^{152}$, ~~and SEQ ID NOS:2-20~~ SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, or SEQ ID NO:20.

14. (currently amended) The composition of Claim 12, wherein said 1 to 100 amino acids is chosen from ~~SEQ ID NOS:22-36~~ SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID:33, SEQ ID NO:34, SEQ ID NO:35, or SEQ ID NO:36.

15. (currently amended) The composition of Claim 12, wherein said 1 to 100 amino acids is chosen from ~~SEQ ID NOS:42-56~~ SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ

ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID:53, SEQ ID NO:54, SEQ ID NO:55, or SEQ ID NO:56.

16. (original) The composition of Claim 1, wherein said amino acid sequence further comprises at least one immune enhancer sequence.

17. (original) The composition of Claim 1, further comprising woodchuck hepatitis virus core antigen chosen from wild type woodchuck hepatitis virus core antigen and modified woodchuck hepatitis virus core antigen lacking a heterologous antigen.

18. (currently amended) A nucleic acid sequence encoding ~~said~~ an antigenic hybrid woodchuck hepatitis virus core antigen, comprising a heterologous antigen linked to inserted within the amino acid sequence set forth in SEQ ID NO:38 ~~of Claim 1.~~

19. (original) An expression vector comprising the nucleic acid sequence of Claim 18.

20. (canceled)

21. (withdrawn) A method, comprising:

- a) providing:
 - i) a mammalian subject; and
 - ii) a composition comprising one or more of a polypeptide comprising a heterologous antigen linked to the amino acid sequence set forth in SEQ ID NO:38, said amino acid sequence comprising a loop region, and an expression vector encoding said polypeptide; and
- b) administering said composition to said subject under conditions such that an immune response is generated.

22. (withdrawn) The method of Claim 21, wherein said immune response comprises one or more of lymphocyte proliferative response, cytokine response and antibody response.

23. (withdrawn) The method of Claim 22, wherein said antibody response comprises production of IgG antibodies.

24. (withdrawn) The method of Claim 23, wherein said IgG antibodies comprise an autoantibody.

25. (withdrawn) A method for producing an immunogenic composition, comprising:

- a) providing:
 - i) a heterologous antigen; and
 - ii) a woodchuck hepatitis virus core antigen set forth in SEQ ID NO 38;
- b) altering at least one of said heterologous antigen and said woodchuck hepatitis virus core antigen, with a modification chosen from insertion of at least one acidic amino acid residue and substitution of at least one acidic amino acid residue;
- c) inserting said heterologous antigen of step b within said hepatitis virus core antigen of step b, to produce a modified woodchuck hepatitis virus core antigen; and
- d) expressing said modified woodchuck hepatitis virus core antigen under conditions suitable for producing particles having a diameter of 25 to 35 nm.

26. (withdrawn) The method of Claim 25, wherein in the absence of said altering, expression of said modified hepatitis virus core antigen yields 25 fold less particles than does expression of a wild type hepatitis virus core antigen.

27. (withdrawn) The method of Claim 25, wherein said at least one acidic amino acid residue comprises at least one aspartic acid residue and at least one glutamic acid residue.

28. (withdrawn) The method of Claim 25, wherein said insertion is in at least one position chosen from the N-terminus and the C-terminus of said heterologous antigen.

29. (withdrawn) The method of Claim 25, wherein said substitution comprises a replacement of at least one non-acidic amino acid residue within said heterologous antigen, with said at least one acidic amino acid residue.

30. (withdrawn) The method of Claim 25, wherein said altering produces a modified heterologous antigen with an isoelectric point in the range of 3.0 to 6.0.

31-35. (canceled)

36. (new) A vaccine comprising a heterologous antigen linked to the amino acid sequence set forth in SEQ ID NO:38.

37. (new) The vaccine of Claim 36, formulated for human administration.

38. (new) The composition of Claim 1, wherein said heterologous antigen further comprises addition of at least one acidic amino acid.

39. (new) The composition of Claim 1, wherein said heterologous antigen comprises a substitution of at least one basic amino acid with at least one acidic amino acid.

40. (new) The composition of Claim 1, wherein said amino acid sequence set forth in SEQ ID NO:38 comprises an insertion of at least one acidic amino acid.

41. (new) The composition of Claim 1, wherein said amino acid sequence set forth in SEQ ID NO:38 comprises a substitution of at least one basic amino acid with at least one acidic amino acid.

42. (new) The vaccine of Claim 36, wherein the isoelectric point of said heterologous antigen is in the range of 3.0 to 6.0.

43. (new) The composition of Claim 38, wherein the isoelectric point of said heterologous antigen is in the range of 3.0 to 6.0.

44. (new) The vaccine of Claim 36, wherein the isoelectric point of said heterologous antigen is in the range of 4.0 to 5.0.

45. (new) The composition of Claim 38, wherein the isoelectric point of said heterologous antigen is in the range of 4.0 to 5.0.

46. (new) The vaccine of Claim 36, wherein the isoelectric point of said heterologous antigen is in the range of 3.0 to 4.0.

47. (new) The composition of Claim 38, wherein the isoelectric point of said heterologous antigen is in the range of 3.0 to 4.0.